201-15009

Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
USA

Gent, 29 December 2003

O/Ref : WH/LP/0822

Dear Administrator:

Attn: Chemical Right-to-Know Program
N-n-Butylbenzenesulphonamide (CAS: 3622-84-2)

On behalf of Proviron Fine Chemicals, I am pleased to submit the Test plan and Robust Summaries for N-n-Butylbenzenesulphonamide (BBSA) under the US High Production Volume (HPV) Challenge Program.

If you require further information, you may contact Vincent Acou at +32.59.56.21.40 or myself.

The submission will also be done electronically to the following e-mail addresses:
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Yours sincerely,

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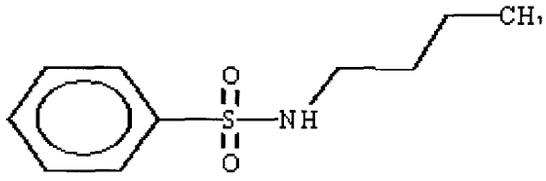
Enclosures: Test Plan, IUCLID data set on CAS 3622-84-2

201-15009

N-n-Butylbenzenesulphonamide



CAS Number 3622-84-2

U.S. EPA HPV Challenge program

December 29, 2003

Submitted by:

Proviron Fine Chemicals

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Executive Overview

N-n-Butylbenzenesulphonamide (BBSA) is a cyclic amide, produced out of the reaction of mono-N-Butylamine (CAS 109-73-9) with Benzenesulphonylchloride (CAS 98-09-9). The synthesis step if followed by a purification, drying and filtration step. BBSA is a clear colourless oily liquid which is almost odourless. It is primarly used as a plasticizer. The product has a low volatility and is practically insoluble in water.

Based on physico-chemical data, the product will not bio-accumulate in the environment (log Pow =2.1). According to the fugacity model, it will be primarly distributed to the soil ad water phase. BBSA will not hydrolyse under normal conditions, and it also proved to be not readily biodegradable.

The toxicity of BBSA to aquatic species is relatively low. The 48h EC50 for Daphnia is 56 mg/l, the 72h ECr50 for algae is 83 mg/l.

The oral LD50 of BBSA is 2070 mg/kg bw and the dermal LD50 is greater than 2000 mg/kg bw which indicate a low acute toxicity. The acute inhalation toxicity (LC50) is greater than 4.066 mg/l after 4 hours of exposure.

In a repeated dose study (28 days), the NOAEL was established at 50 mg/kg/day.
An *in vitro* genetic toxicity study showed that there is no mutagenic potential in the presence or absence of metabolic activation.

There were no studies available on *in vivo* genetic toxicology or on reproductive or developmental toxicity.

It is concluded that additional studies are needed for *in vivo* genetic toxicology and for reproductive or developmental toxicity. Two studies are recommended, OECD 473 (Chromosome aberration Test) and OECD 421 (Combined Reproduction / Developmental Screening Test), to fill the data elements of the HPV.

Data analysis

CAS Number 3622-84-2 **N-Butylbenzenesulphonamide**	**Available**	**Estimation Method**	**Acceptable**	**Testing Recommended**
HPV endpoint				
Physical Chemical data				
Melting Point	Y		Y	N
Boiling Point	Y		Y	N
Vapor Pressure	Y		Y	N
Partition coefficient (octanol/water)	Y		Y	N
Environmental Fate				
Photo-Degradation		Y	Y	N
Abiotic Degradation-Hydrolysis	Y		Y	N
Biodegradation	Y		Y	N
Transport		Y	Y	N
Ecotoxicity				
Acute toxicity to Fish		Y	Y	N
Acute toxicity to Daphnia	Y	Y	Y	N
Acute toxicity to Algae	Y	Y	Y	N
Toxicity				
Acute toxicity	Y		Y	N
Repeated dose	Y		Y	N
Genetic toxicology in vitro	Y		Y	N
Genetic toxicology in vivo				Y
Reproductive Toxicity				Y
Developmental Toxicity				Y

Introduction

N-n-Butylbenzenesulphonamide (BBSA) is a clear, colourless, almost odourless oily liquid.
BBSA is used as a plasticizer in polyacetals, polycarbonates, polysulphones and in Nylon 11 and Nylon 12. As a plasticizer, it contributes the following properties on the above materials:

- easier removal from the mould
- easier machining
- a better finish due to more regular pore-size distribution
- good heat stability up to 180°C, and, in particular, a barrier to the absorption of water, whence an outstanding shape stability

Polyamide 11 and 12 compounds, containing BBSA, are used for flexible tubing used for example in flexodrilling. The extruded materials are distinguished by higher impact strength at low temperatures.
Another specific application of flexible polyamide tubing is the manufacture of compressed-air brake hoses for most heavy commercial vehicles.
Exposure is limited by process conditions, and controlled by using efficient exhaust when used at high temperature. No occupational exposure level set by a governmental organisation could be found for BBSA.
Common synonyms are N-n-Butylbenzenesulfonamide and N-n-Butylamide of benzenesulphonic acid.

Physicochemical data

Physicochemical data are available from tests done by the manufacturer or contract laboratories.

Table 1: Physicochemical properties	
Melting Point	-30°C
Boiling Point	> 250°C (1013 hPa)
Vapour Pressure	<0.001 hPa (20°C)
Octanol-Water Partition coefficient	Log Ko/w = 2.1 (8)
Water solubility	1.02 g/l (20°C)

These properties indicate that N-Butylbenzenesulphonamide is an involatile liquid, practically insoluble in water. The log Ko/w is smaller than 3, this indicates that there is a low potential for bioaccumulation.

Recommendation

The physico-chemical properties are well defined. No additional testing is needed for physico-chemical properties.

Environmental Fate

Photodegradation

The photodegradation rate was calculated using AOPWIN v1.90 (Atmosperic Oxidation Program for Microsoft Windows) (3) that estimates the rate constant for the atmosheric, gas-phase reaction between organic chemicals and photochemically produced hydroxyl radicals. The estimated rate constant is then used to calculate atmospheric half-life values for organic compounds based upon average atmospheric concentrations of hydroxyl radicals. AOPWIN calculated a rate constant of 13.83 E-12 cm^3/molecule.sec.
Modeling the $T_{1/2}$ for the reaction of N-Butylbenzenesulphonamide with atmospheric hydroxyl radical at the EPA-accepted default concentration of 1,500,000 radicals per cubic centimeter results in an estimate of relatively short half-lives in air (9.28 hours)

Stability in water – Hydrolysis

Sulfonamides (like N-Butylbenzenesulphonamide) do not hydrolyse under normal condition (neutral aqueous environment) (1)

Transport between Environmental Compartments

The fugacity of N-Butylbenzenesulphonamide in the environment was estimated using the Mackay's EQC Level III Fugacity Model with the default values available in EPIWIN v3.10 (3). The measured log Ko/w (2.1) was used for the calculation. The results for distribution using equal initial distribution to air, water soil and sediment are (in percent mass amount):

- Air 2.39%
- Water 42.3%
- Soil 55.2%
- Sediment 0.14%

EQC modeling predicts that the majority of the substance will be in the soil and water phase.

Biodegradation

Determination of the ready biodegradability has been done by the Carbon Dioxide (CO2) Evolution Test (Modified Sturm Test).(9) The average degradation values during the test period revealed 18% degradation.
N-Butylbenzenesulphonamide was not readily biodegradable under the conditions of the modified Sturm test.
In the toxicity control the substance was found not to be inhibitory.

Recommendation

No further tests on environmental fate are recommended.

Ecotoxicity

Acute Fish toxicity

No experimental data are available. The ECOSAR program predicts an acute toxicity value of 80.8 mg/l (LC50, 96h).

Acute Daphnia toxicity

An acute toxicity study in Daphnia magna (static) with N-Butylbenzenesulphonamide is available. (6) Under the conditions of the study, the product did not induce acute immobilisation of Daphnia magna at 32 mg/l after 48 hours of exposure (NOEC). The 48h-EC50 was 56 mg/l based on nominal concentrations (95% confidence interval between 49 and 69 mg/l).

Freshwater Algae inhibition

A Fresh water algae growth inhibition test is available for N-Butylbenzenesulphonamide. (10) Under the conditions of the study with Selenastrum capricornutum, the NOEC for cell growth inhibition was determined to be 22 mg/l and the NOEC for growth rate reduction was 10 mg/l. The EC50 for cell growth inhibition (EbC50:0-72h) was 49 mg/l. The EC50 for growth rate reduction (ErC50:0-72h) was 83 mg/l.

The U.S. EPA has developed a SAR relationship for aquatic toxicity that shows a good correlation for this compound in relation with experimental data for Daphnia and Algae toxicity.
In Table, the values from experimental data and ECOSAR predictions are listed.

Table 2: SAR and experimental toxicity values		
	Experimental values	ECOSAR Prediction (3)
Fish, LC50 (96h)	-	80.8 mg/l
Daphnia, EC50 (48h)	56 mg/l	88.5 mg/l
Algae, EC50 (72h)	49 mg/l	56.3 mg/l

Recommendation

From the table it can be concluded that the predictions from ECOSAR are very close to the experimental values. N-Butylbenzenesulphonamide is most toxic to freshwater algae. According to ECOSAR, the toxicity to Fish lies between the toxicity to Algae and the toxicity to Daphnia. The data available from SAR and experimental toxicity values fill the HPV required endpoints. It is recommended that no additional studies be conducted.

Health effects

Acute toxicity

Study reports on acute toxicity are available for N-Butylbenzenesulphonamide.
The acute oral toxicity study on rats reported an LD50 of 2070 mg/kg bw. (5)
Acute dermal toxicity is measured in rats and indicates an LD50 greater than 2000 mg/kg bw.(4)
A study according to OECD Guideline 403 "Acute Inhalation Toxicity" is available. The study was performed with N-Butylbenzenesulphonamide 99.8% grade. The LC50 to rats after 4 hours exposure is greater than 4.066 mg/l. The N-Butylbenzenesulphonamide concentration at saturation (in air): 0.06 μg/l at 20°C.(2)

Repeated Dose Toxicity

For N-Butylbenzenesulphonamide oral, dermal and inhalation are considered to be possible exposure routes. As the substance is an involatile fluid, the inhalation route is expected to be less relevant. Therefore an oral 28-day toxicity study according to OECD 407 was performed. (11)
The dose levels for the 28-day study were selected to be 0, 50, 150 and 1000 mg/kg/day.
All high dose animals died prior to their scheduled necropsy. Up to 150 mg/kg/day the animals survived up to there scheduled termination.
High dose animals showed lethargy, hunched posture, uncoordinated movements, abnormal gait, salivation, emaciation, laboured respiration, swelling of the abdomen or head, and/or piloerection prior to sacrifice/death. All males

and most females of the high dose lost weight (up to 30%) or showed reduced weight gain and showed reduced food intake.
Degenerating nerve fibers were observed at low incidence and severity in the spinal cord and sciatic nerves at 150 and 1000 mg/kg/day. At 150 mg/kg/day, post mortem findings were confined to liver enlargement and hepatocyte hypertrophy, thymic atrophy and lymphocytolysis.
At 50 and 150 mg/kg/day, there were no changes at performance of functional observations, body weight and food consumption measurements, or alterations during clinical biochemistry investigations that were considered to be an effect of treatment. Also, at 50 mg/kg/day there were no treatment related macro- or microscopic findings.
The No Observed Adverse Effect Level (NOAEL) was established at 50 mg/kg/day.

Recommendation

No additional repeated dose studies are recommended.

Genetic Toxicity

Genetic Toxicology in vitro

An Ames metabolic activation test is available that assesses the potential mutagenic effect of the substance N-Butylbenzenesulphonamide.
It is concluded that no evidence of mutagenic potential was obtained in this bacterial (Salmonella typhimurium) test system in the presence or absence of metabolic activation. (7)
Genetic Toxicology in vivo

No data are available

Recommendation

It is recommended to perform a Chromosome aberration test (OECD Guideline 473)

Reproductive Toxicity

No studies are available

Developmental Toxicity

No studies are available

Recommendation
No data are available on reproductive or developmental toxicity. Therefore it is recommended to perform a Reproduction / Developmental Toxicity Screening Test, according to OECD 421.

Conclusion

With regard to the parameters demanded in the EPA HPV Challenge program, the available data fill the requirements for physicochemical, environmental fate and ecotoxicological parameters. Additional studies in these areas would not add significantly to our understanding of this material. For mammalian toxicity 2 tests are recommended, OECD 473 (Chromosome Aberration test) and OECD 421 (Reproduction / Developmental Screening test).

References

1. Advanced Organic Chemistry, Jerry March, 4th edition
2. BAYER, Fachbereich Toxicologie: Untersuchungen zur Akuten Inhalationtoxizität an der Ratte (Studien-Nr: T9037171 und T8039718), 1991
3. EPIWIN: The SRC PhysProp Database, 2000.
4. Proviron Fine Chemicals NV: Acute Dermal Toxicity to the Rat (Huntingdon Life Sciences Ltd. Report No. UCB 566/951936/AC), 1995
5. Proviron Fine Chemicals NV: Acute Oral Toxicity to the Rat (Huntingdon Life Sciences Ltd. Report No. UCB 565/952011/AC), 1996
6. Proviron Fine Chemicals NV: Acute Toxicity Study in Daphnia magna with BBSA (static) (NOTOX Project 312121), 2001
7. Proviron Fine Chemicals NV: Ames Metabolic Activation Test to Assess the Potential Mutagenic Effect of N-Butylbenzenesulphonamide (HRC Report NO. UCB 180/83524), 1983
8. Proviron Fine Chemicals NV: Calculation of the Partition Coefficient (N-Octanol/Water) of BBSA (NOTOX Project 312132), 2001
9. Proviron Fine Chemicals NV: Determination of 'Ready' Biodegradability: Carbon dioxide (CO2) Evolution Test (Modified Sturm Test) with BBSA (NOTOX Project 312108), 2001
10. Proviron Fine Chemicals NV: Fresh Water Algal Growth Inhibition Test with BBSA (NOTOX Project 312119), 2001
11. Proviron Fine Chemicals NV: Subacute 28-day Oral Toxicity with BBSA by Daily Gavage in the Rat (NOTOX Project 354149), 2003

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I U C L I D

Data Set

Existing Chemical	:	ID: 3622-84-2
CAS No.	:	3622-84-2
EINECS Name	:	N-butylbenzenesulphonamide
EC No.	:	222-823-6
TSCA Name	:	Benzenesulfonamide, N-butyl-
Molecular Formula	:	C10H15NO2S

Producer related part

Company	:	Proviron Fine Chemicals N.V.
Creation date	:	13.08.2003

Substance related part

Company	:	Proviron Fine Chemicals N.V.
Creation date	:	13.08.2003
Status	:	
Memo	:	HPV Challenge Program
Printing date	:	29.12.2003
Revision date	:	
Date of last update	:	29.12.2003
Number of pages	:	20
Chapter (profile)	:	Chapter: 1.0.1, 1.0.2, 1.0.3, 1.0.4, 1.1.0, 1.1.1, 1.2, 1.6.1, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 2.7, 3.5, 4.1, 4.2, 4.3, 5.0, 5.1.1, 5.1.2, 5.1.3, 5.4, 5.5, 5.9
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Proviron Fine Chemicals N.V.
Contact person	:	Vincent Acou
Date	:	
Street	:	Stationsstraat 123 bus 2
Town	:	8400 Oostende
Country	:	Belgium
Phone	:	+32 59 56 21 00
Telefax	:	+32 59 56 21 30
Telex	:	
Cedex	:	
Email	:	vincent.acou@proviron.com
Homepage	:	

21.06.2001

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	manufacturer
Name of plant	:	Proviron Fine Chemicals N.V.
Street	:	Stationsstraat 123 bus 2
Town	:	8400 Oostende
Country	:	Belgium
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

21.06.2001

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	
Molecular formula	:	C10H15NO2S
Molecular weight	:	213.3
Petrol class	:	

21.06.2001

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	

Substance type	:	organic
Physical status	:	liquid
Purity	:	>= 99 % w/w
Colour	:	
Odour	:	

10.12.2003

1.2 SYNONYMS AND TRADENAMES

BBSA; n-Butylamide of benzenesulphonic acid

14.05.1998

1.6.1 LABELLING

Labelling	:	provisionally by manufacturer/importer
Specific limits	:	

10.12.2003

2.1 MELTING POINT

Value	:	< -30 °C
Sublimation	:	
Method	:	other: ISO 1392
Year	:	1991
GLP	:	no
Test substance	:	

14.05.1998

2.2 BOILING POINT

Value	:	> 250 °C at 1013 hPa
Source	:	Proviron Fine Chemicals N.V. Oostende

10.12.2003

2.3 DENSITY

Type	:	relative density
Value	:	ca. 1.147 g/cm³ at 20 °C
Method	:	other: ISO 758
Year	:	1991
GLP	:	no
Test substance	:	

14.05.1998

2.4 VAPOUR PRESSURE

Value	:	.56 hPa at 184 °C
Decomposition	:	
Method	:	
Year	:	1954
GLP	:	no
Test substance	:	

Source	:	Proviron Fine Chemicals N.V. Oostende

14.05.1998

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 2.1 at °C
pH value	:	
Method	:	other (calculated)
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	Rekker calculation method
Source	:	Proviron Fine Chemicals

21.11.2003

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	ca. 1.02 at 20 °C
pH value	:	ca. 6.7
concentration	:	1.02 g/l at 20 °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	

21.11.2003

2.7 FLASH POINT

Value	:	>= 200 °C
Type	:	open cup
Method	:	other: ISO 2719
Year	:	1991
GLP	:	no
Test substance	:	

14.05.1998 (3)

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge
Concentration	:	21.5 mg/l related to Test substance related to
Contact time	:	
Degradation	:	ca. 18 (±) % after 28 day(s)
Result	:	
Control substance	:	other
Kinetic	:	% %
Deg. product	:	
Method	:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	In the toxicity control more than 25% degradation occured within 14 days (based on ThCOé). Therefore, the test substance was assumed to be not inhibitory.
Result	:	The substance was not readily biodegradable under the conditions of the performed modified Sturm test.
Source	:	Proviron Fine Chemicals
Reliability	:	(1) valid without restriction
Flag	:	confidential

21.11.2003

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 56 measured/nominal
Method	:	OECD Guide-line 202
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Proviron Fine Chemicals
Reliability	:	(1) valid without restriction
Flag	:	confidential

21.11.2003

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 10
EC50	:	= 83 measured/nominal
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The EC50 for cell growth inhibition was 49 mg/l, the NOEC was determined to be 22 mg/l.
Source	:	Proviron Fine Chemicals
Reliability	:	(1) valid without restriction
Flag	:	confidential

21.11.2003

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 2070 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Method	:	Directive 92/69/EEC, B.1
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction
Flag	:	confidential

10.12.2003 (4)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 4.066 mg/l
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1991
GLP	:	yes
Test substance	:	other TS: BBSA 99.8% grade
Remark	:	BBSA concentration at saturation (in air) : 0.06 ug/l at 20°C
Flag	:	confidential

14.05.1998 (1)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Method	:	Directive 92/69/EEC, B.3
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction

Flag : confidential
10.12.2003 (5)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	28 Days
Frequency of treatm.	:	Daily
Post exposure period	:	
Doses	:	0-50-150-1000 mg/kg/day
Control group	:	yes
NOAEL	:	= 50 mg/kg
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result : The high dose of 1000 mg/kg/day resulted in the deth or moribund state of all rats. Clinical signs shown by these animals prioe to death/sacrifice included lethargy, hunched posture, uncoordinated movements, abnormal gait, salivation, emaciation, laboured respiration, swelling of hte abdomen or head and piloerection.
Examination revealed liver enlargement and hepatocyte hypertrophy, liver necrosis, hyaline droplets formation in the renal papillary collecting ducts, adrenal gland enlargement with fatty change or cortical hypertrophy and reduced size and/or arophy of the thymus, spleen and male reproductive organs.
At 150 mg/kg/day, post-mortem findings were confined to liver enlargement and hepatocyte hypertrophy, thymic atrophy and lymphocytolysis.
Cortical hyaline were noted in the kidneys of most male rats dosed at 50 mg/kg/day and above. This is a specific male rat response and is not observed in female rats or higher species of either sex.
Degenerating nerve fibres were observed at low incidence and severity in the spinal cord and sciatic nerves at 150 and 1000 mg/kg/day.
At 50 and 150 mg/kg/day, there were no changes at performance of functional observations, body weight and food consumption measurements.
At 50 mg/kg/day there sere no treatment related macro- or microscopic findings.

Source	:	Proviron Fine Chemicals
Conclusion	:	A No Observed Adverse Effect Level (NOAEL) of 50 mg/kg/day was established (excluding the presence of hyaline droplets in male kidneys).
Reliability	:	(1) valid without restriction
Flag	:	confidential

21.11.2003

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	salmonella typhimurium
Test concentration	:	5, 50, 500 and 5000 ug/plate. Strains : TA1535, TA1537, TA1538, TA98 & TA100
Cycotoxic concentr.	:	

Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1983
GLP	:	no
Test substance	:	other TS: UCB 99.5% grade
Flag	:	confidential

14.05.1998 (2)

(1) BAYER AG, Fachbereich Toxikologie; unpublished study T9037171/T 8039718; 04.01.1991 (joint property BAYER/UCB)

(2) HRC UCB 180/83524 (1983)

(3) Proviron Fine Chemicals N.V. Oostende

(4) UCB 565/952011/AC

(5) UCB 566/951936/AC